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(71) Applicants: ROCHE DIAGNOSTIC GMBH [DE/DE]; 68298 Mannheim (DE). STEAG MICROPARTS GMBH [DE/DE]; Hauert 7, 44227 Dortmund (DE). ROCHE DIAGNOSTICS CORPORATION [US/US]; 9115 Hague Road, P.O. Box 50457, Indianapolis, IN 46250-0457 (US).

(72) Inventors: MACHO, Heinz; Fahrenbacher Str. 142, 64658 Fuerth (DE). GERLACH, Torsten (deceased). BHULLAR, Rhagbir, Singh; 6130 Chadsworth Way, Indianapolis, IN 46236 (US). SCHOEN, Christian; Baroper Kirchweg 36, 44227 Dortmund (DE). PETERS, Ralf-Peter; Zum Waschbach 23a, 51467 Bergisch Gladbach (DE).

(74) Common Representative: ROCHE DIAGNOSTICS GMBH; Patent Department, 68298 Mannheim (DE).

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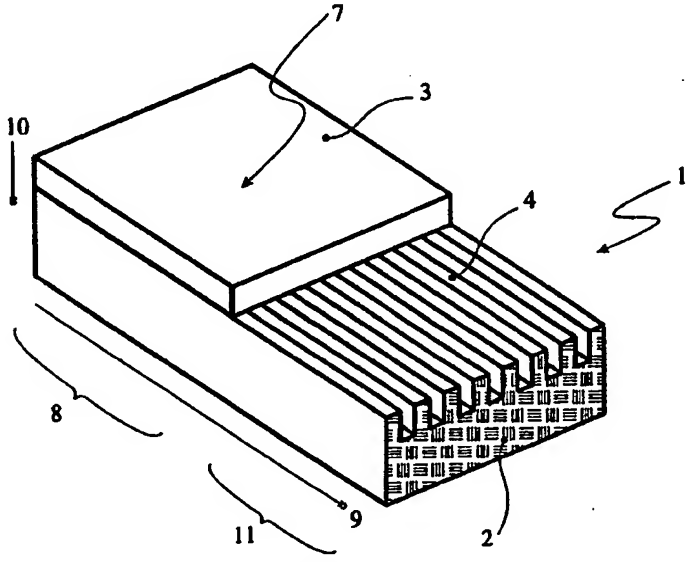


(57) Abstract: The present invention concerns analytical test elements such as test carriers for examining a liquid sample. The analytical test elements according to the invention comprise a first and a second capillary-active zone which are in contact with one another to enable liquid transfer. The capillarity of the first capillary-active zone is caused by a capillary-active porous matrix material. The second capillary-active zone comprises one or several capillary channels or gaps which are at least partially overlapped by the porous matrix material of the first capillary-active zone. A system which comprises such an analytical test element and a suitable measuring instrument is also disclosed. The invention also concerns a method for separating undesired sample components from a liquid sample and a method for analyte detection wherein each method utilizes such analytical test elements.

WO 01/24931 A1

CAPILLARY DEVICE FOR SEPARATING UNDESIRED COMPONENTS FROM A LIQUID SAMPLE AND RELATED METHOD

The present invention concerns analytical test elements such as test carriers for examining a liquid sample. The analytical test elements according to the invention contain a first and a second capillary-active zone which are in contact with one another enabling liquid transfer. According to the invention the capillarity of the first capillary-active zone is caused by a capillary-active porous matrix material. The invention additionally concerns a method for separating undesired sample components from a liquid sample and a method for analyte detection which both utilize the analytical test elements according to the invention.

Carrier-bound rapid tests have become established for the chemical and biochemical analysis of solid and liquid sample materials in specialised laboratories but also especially for use outside laboratories. Such carrier-bound rapid tests based on a specially developed dry chemistry are simple and uncomplicated to carry out even by laymen despite the often complex reactions involving sensitive reagents. The most prominent example of carrier-bound rapid tests are test strips for the determination of the blood glucose content in diabetics. Single or multiple zone test strips for urine analysis and diverse indicator papers are also well-known. Since, in addition to rapid tests in a strip form (test strips), there are also other forms of carrier-bound rapid tests, they are generally referred to as "analytical test elements".

Many sample materials that are to be examined with the aid of analytical test elements are complex mixtures of different constituents. This applies especially to samples of biological liquids and body fluids. Only a few of the constituents of these samples can be used for the actual determination of an analyte or to evaluate the state of a sample. The majority of the remaining components usually do not have an adverse effect on the detection reaction of the target analyte. Nevertheless it may be necessary to separate parts of the sample material from the sample before the detection reaction since these parts may influence or interfere with the detection reaction or the result of the detection reaction may be difficult or impossible to detect in the presence of these components.

Especially when blood is used as a sample material the problem arises that the pigment hemoglobin contained in the red blood corpuscles (erythrocytes) interferes greatly with optical detection methods for blood components such as e.g. blood glucose, cholesterol etc. Hence in the prior art there is no lack of methods for obtaining almost colorless plasma or serum from blood by separating the cellular components and in particular by separating the colored erythrocytes.

The classical separation of plasma from whole blood by centrifugation utilizes the density differences of plasma and blood cells. During centrifugation, different centrifugal forces act on the plasma on the one hand and on blood cells on the other hand which in turn lead to a spatial separation of the blood cells from the plasma. After the centrifugation, the plasma is available more or less separate as a supernatant, for example, for further processing or for subsequent diagnostic

reactions. A disadvantage of this method is the elaborate apparatus that is required and the many handling steps. This type of plasma isolation can only be carried out in a suitable laboratory by technical personnel. This method is unsuitable for modern analytical test elements.

Various materials are known which can be used in analytical test elements to separate blood cells from whole blood. German Patent Specification DE 30 29 579 C2 describes for example the use of glass fiber fleeces for separating plasma or serum from whole blood and diagnostic means (test strips) in which such glass fiber fleeces or papers are placed in front of a porous reaction layer. Special embodiments of the diagnostic means disclosed in DE 30 29 579 C2, e.g. shown in Figs. 3-5, describe a sample application on a chromatographic material, essentially horizontal transport of the sample in the material to a detection layer and subsequent vertical transport into the detection layer.

A glass fiber fleece for isolating plasma is also used in an analytical test element in European Patent Application EP-A 0 470 438. In this case, the blood sample passes through a capillary channel which has a dosing function into a glass fiber fleece where erythrocytes are separated. From there the plasma obtained in this manner is transferred directly into a reaction layer, for example a membrane, where the detection reaction takes place.

European Patent Application EP-A 0 408 222 discloses a test element in which a separation membrane is used to separate desired and undesired sample components. Sample

liquid is applied to the test element and transported in a capillary gap to the separation membrane. Here the sample is freed of undesired accompanying substances and subsequently transferred to a detection layer which is in contact with the membrane where optionally a detection reaction takes place.

A disadvantage of the test elements according to DE 30 29 579 C2, EP-A 0 470 438 and EP-A 0 408 222 is that the plasma obtained is bound immediately after the isolation by a porous material and thus cannot be utilized for transmission and/or scattered light measurements. Moreover, it is difficult to divide the plasma into several portions in order, for example, to carry out determination reactions at several sites in the test element and thus in order to determine several parameters from one sample.

U.S. Pat. No. 5,458,852 describes a transparent analytical test element in which a filter element can be included to separate plasma from blood in the sample application zone. One side of this zone is adjoined by a zone which is capillary-active due to capillary channels and in which, among others, the detection reaction for the target analyte takes place. Since only the edge of the filter element is in contact with the capillary channels, the plasma can only be transported slowly from the filter element. As described in U.S. Pat. No. 5,458,852, this may be an advantage if a controlled incubation of the sample is desired, for example, in immunological methods of determination. However, this is a disadvantage for most non-immunological test elements since the total analytical period is unnecessarily long due to the slow transfer of the sample from the filter element into the detection zone.

U.S. Pat. Nos. 4,753,776 and 5,135,719 describe analytical devices that use a filter medium for separating plasma or serum from whole blood. A whole blood sample applied to the device passes through the filter medium. There, red blood cells are separated from the whole blood sample to produce plasma or serum. The resulting plasma or serum is collected in a chamber underneath the filter medium. From there, the plasma or serum is drawn into capillaries for further investigation. Since the filter medium itself is only in contact with the serum or plasma collection chamber and not in direct contact with the capillary active zone of the device, serum or plasma is taken up by the capillaries only after enough serum or plasma is present in the collection chamber. This may lead to a delay in transporting the serum or plasma into the capillaries, and thus to a delay in carrying out subsequent analytical reactions.

What was said above in connection with blood about the separation of serum or plasma or removal of cellular components by filtration applies analogously to other sample materials and other interfering sample components.

The object of the invention is to eliminate the disadvantages of the prior art. In particular the object of the present invention is to provide a simple analytical test element which, without further help from a user, separates undesired sample components after application of a liquid sample to the analytical test element and rapidly makes the remaining liquid sample available for subsequent measurements optionally in connection with analytical detection reactions. In particular, measurements should be possible which can

detect the optical properties of the sample freed of the undesired components or changes in these properties.

This object is achieved by the present invention. The invention concerns an analytical test element for examining a liquid sample, the test element comprising a first and a second capillary-active zone which are in contact with one another enabling a liquid transfer where the capillarity of the first capillary-active zone is caused by a capillary-active porous matrix material. An essential feature is that the capillarity of the second capillary-active zone is not due to the porosity of a matrix material but it is a result of the fact that it contains one or several capillary gaps or channels. These gaps or channels are at least partially overlapped by the porous matrix material of the first capillary-active zone.

It was surprisingly found that liquid can pass from the first into the second capillary-active zone when the capillarity of the second zone is larger than that of the first zone and also when the capillarity of the second capillary-active zone is equal to or smaller than that of the first zone. However, in the latter case the liquid sample should not be completely absorbed into the material of the first zone. Instead it is necessary in this case that an excess of sample remains on the porous material of the first zone.

Analytical test elements in the sense of the invention are understood as devices which typically are adapted to absorb or contain sample liquids and are able to make them available for a simultaneous or later analysis. For example, suitable detection reactions can already occur

in the analytical test elements during or after uptake of the sample liquid which allow determination of the presence or amount of an analyte in the sample. Analytical test elements in the sense of the invention can, however, also be cuvettes which only serve as a receptacle for the samples in which the analysis is carried out without subsequent reactions. The analytical test elements can of course also be used to store and keep sample liquids. However, they are preferably test strips that can be evaluated visually or optically by means of an apparatus. In other words, the analytical test elements can be electrochemical or optical biosensors and the like.

In principle, the analytical test element according to the invention is suitable for analyzing any type of sample liquid. Sample liquids in the sense of the invention are liquids which are to be examined with regard to one or several of their components or properties with the aid of the analytical test element according to the invention. Sample liquids are in particular typically aqueous liquids in which the presence or the content of one or several dissolved or suspended components are to be determined. Sample liquids in the sense of the invention are particularly preferably body fluids such as e.g. blood, urine, saliva, sweat, etc. as such or in a derived form such as e.g. serum or plasma. Sample material from the environment such as water and sludge samples, sample material from technical processes such as fermentation broths, liquid and liquefied foods, drinks and so-on are also suitable in the sense of the invention as sample liquids although less preferred. The component or components whose presence or content is to be examined

in the sample liquid is or are named analyte(s) or target analyte(s).

The test element according to the invention is characterized in that it has at least two capillary-active zones. Capillary-active zones or capillary zones within the meaning of the invention are zones which, as a result of capillary properties, i.e. capillarity, are able to take up liquids and in particular polar, aqueous liquid samples as a result of capillary forces and optionally to store them or to transport them.

In this connection, an essential feature of the invention is that the capillarity of the first zone is caused by the porous structure of a capillary-active matrix material, for example a paper, fleece, fabric, knitted fabric or a membrane. In contrast, the capillarity of the second capillary-active zone is not due to the capillarity of a porous matrix material. The capillarity of the second capillary-active zone results from essentially ordered capillary gaps or capillary channels.

Capillary gaps within the meaning of the invention are understood as geometric structures in which the distance between at least two substantially planar and parallel inner surfaces is small enough to have a capillary-active effect. For example, two plane, parallel glass plates or stiff plastic foils which have a gap between each other of a few hundred micrometers (µm) can form a capillary gap.

In the case of the present invention, capillary channels should be geometric structures in which more than two

inner surfaces are spaced at such small distances that capillarity is induced. Capillary channels can for example be grooves or troughs of small depth and width in a planar material. However, capillary channels can also be tubes of a small diameter in which case the cross-section of the tubes can in principle be any shape but preferably a regular or irregular rectangle, ellipsoid or circle.

In order to have a capillary-active effect for aqueous sample liquids, it has proven to be advantageous that the distance between at least two inner surfaces of the capillary gaps or channels is at most about 200 micrometers (µm). The distance is preferably about 100 micrometers (µm). The distance should not be less than about 1 micrometer (µm) to avoid the entrapment of gas bubbles in the capillary gaps or channels.

The terms "capillary gap" and "capillary channel" are to be regarded as synonymous in relation to the present invention. The capillarity in the second zone of the test element is due to a capillary gap or a capillary channel, and the capillarity in the first zone is caused by a porous, capillary-active matrix material.

Suitable porous matrix materials for the first capillary-active zone are for example fleeces, papers, fabrics, or knitted fabrics made of natural or synthetic organic or inorganic fibrous materials. Layers containing membranes, sponges, wicks, foamed materials, adsorbents such as silica gel or aluminium oxide and so-on are also suitable. It is also possible for the first capillary-active zone to contain several different matrix materials mentioned above, for example, a

laminate composed of a membrane and a fleece or a membrane and a layer coated thereon or a film made of an adsorbent. The porous matrix material is preferably a fleece, fabric or a membrane. The liquid transport in the matrix material or matrix materials is essentially due to capillary forces.

The capillary-active porous matrix material of the first capillary-active zone is preferably able to separate undesired sample components such as colored sample components or interfering particulate sample components from the sample liquid. The porous material at the same time acts as a filter or sieve. In particular, it is preferable that the porous matrix material is able to separate plasma or serum from a whole blood sample.

For this purpose, the capillary-active porous matrix material can be a suitable membrane as disclosed for example in European Patent Application EP-A-0 336 483 or a glass fiber fleece such as that known from German Patent Application DE-A 30 29 579. The capillary-active porous matrix material of the first capillary-active zone is particularly preferably a plasma separation membrane, in particular a polyether-sulfone-polyvinyl-pyrrolidone membrane which is for example distributed by the PrimeCare B.V. Company of The Netherlands.

The second capillary-active zone of the analytical test element according to the invention is preferably manufactured from an injection-molded part which contains capillary structures (capillary channels and/or capillary gaps) and in particular very small, so-called microcapillary structures. This injection molded part is particularly preferably composed of a transparent

plastic. Suitable plastics which can be injection molded are familiar to a person skilled in the art. Examples are polyethylene (PE), polypropylene (PP), polycarbonate (PC), poly(ethylene terephthalate) (PET) and so-on.

In an alternative embodiment, the second capillary-active zone can comprise a carrier material in which capillary structures and in particular microcapillary structures have been stamped or etched. Suitable carrier materials include a number of materials which are usually used to manufacture analytical test elements such as metal or plastic foils, coated papers or cardboards, and glass. The carrier is preferably manufactured from a transparent plastic foil such as polyethylene, polypropylene, poly(ethylene terephthalate) or polycarbonate.

In a further preferred embodiment, the second capillary-active zone comprises a substantially flat, smooth carrier material on which structures have been applied which define the capillaries. For example the structures can be applied to the carrier material in the form of thin lines or minute projections. The structures can for example consist of discrete areas of hot-melt adhesive as is known from European Patent Application EP-A 0 297 389 or European Patent Application EP-A 0 297 390. It is, however, also possible to use other forms of polymeric materials such as plastic foils or polymer fibers to create the structures such as by lamination onto the carrier material. It is also possible to print the carrier material with capillary structures. The structures can be applied regularly or irregularly on the carrier material. The capillary areas produced by these structures are formed so that they are in communication.

According to the invention, the second capillary-active zone in the analytical test element is at least partially covered or overlapped by the first capillary-active zone. The capillary-active porous material of the first capillary-active zone can for example partially be a boundary area of the capillary gap or the capillary channels of the second capillary-active zone. The capillary-active porous material of the first capillary-active zone is preferably in direct contact with the second capillary-active zone. An overlap of the two zones ensures a rapid and effective transport of the sample liquid from the first capillary-active zone into the second capillary-active zone.

In a preferred embodiment, the capillary channel or capillary channels or gaps of the second capillary-active zone can be open at least in the area in which they are covered or overlapped by the material of the first capillary-active zone. This allows liquid to pass through the openings from the first capillary-active zone into the second capillary-active zone. For example, the capillary channels can be open at the top if the porous matrix material lies on the second capillary-active zone. In this connection, the matrix material of the first capillary-active zone is particularly preferably in intimate contact with the second capillary-active zone to facilitate liquid exchange between the zones.

To achieve an adequate capillarity, it is preferred according to the invention that the surface of the capillary gaps of the second capillary-active zone be made of materials which exhibit a hydrophilic character, such as glass, or which are at least partially hydrophilized, i.e., hydrophilically modified.

Hydrophilic surfaces are characterized by a good wettability by water or water-like liquids or solutions. They in general possess a high surface tension which is near the surface tension of water which is approximately 0.072 Newtons per meter (N/m). Hydrophilic modification of plastic surfaces can be accomplished by use of corona plasma treatment, plasma chemical vapor deposition (PACVD, for example, with the assistance of Antec Co.of Kelkheim, Germany), covalent binding of photoreactive hydrophilic polymers on a plastic surface (Photo Link Surface, for example, with the assistance of BSI Corporation Co., Eden Prairie, Minnesota), application of layers containing wetting agents on a plastic surface (for example, with the assistance of Adhesive Research Co., Glen Rock, Pennsylvania, USA) or coating inorganic-organic nanocomposites using sol-gel technology on the surfaces to be modified (for example, with the assistance of INM Co.of Saarbrücken, Germany). The coating of surfaces with oxidized metal layers such as oxidized aluminium layers known from German Patent Application DE-A 197 53 848.7 is also suitable for increasing the hydrophilicity of plastic surfaces.

The analytical test element according to the invention is characterized in a further embodiment by the second capillary-active zone containing regions of different capillarity. This enables the creation of successive regions of increasing capillarity in the second capillary-active zone in the direction of transport of the sample liquid. This can for example be achieved by reducing the distance between two surfaces determining the capillarity. It is, however, also possible according to the invention that in the second capillary-active zone there are successive regions of decreasing capillarity in the direction of transport of the sample

liquid. This can for example be achieved by special constructions as for example disclosed in U.S. Pat. No. 5,458,852. In addition, it is also possible that there is firstly an increase of capillarity in the direction of transport of the sample liquid and subsequently a decrease of the capillarity or vice versa in the second capillary-active zone.

The liquid transport in the first capillary-active zone is preferably essentially perpendicular to the liquid transport in the second capillary-active zone. For example, the liquid can be transported vertically in the first zone, i.e., parallel to the direction of gravity. In this case, the liquid is transported horizontally in the second zone. Of course, the reverse is also possible.

Although according to the invention it is possible that the analytical test element only has one capillary channel or gap in its second capillary-active zone, it is preferable that the second capillary-active zone has a plurality and in particular a plurality of parallel capillary channels or gaps. This ensures that for the total number of capillaries in the second capillary-active zone, the ratio of the capillary circumference to the cross-section of the capillaries or, in other words, of the inner surface of the capillaries to their volume is large. It is assumed that the resulting high capillary force has the effect that liquid which is at first more or less bound in the first capillary-active zone readily passes into the second capillary-active zone.

The capillary channels (or gaps) of the second capillary-active zone can be arranged randomly in a plane. The capillary channels can be easily directed in various directions away from the first capillary-active zone in order to achieve a liquid transport in various directions. This can for example be advantageous for test elements which are used to determine several analytes from one and the same sample. In this case, the capillary channels can supply different detection zones with sample liquid whereby it is possible to supply each of the detection zones with identical or individually different amounts of sample liquid. The amount of sample liquid can for example be regulated by the number of individual capillary channels or their volumes. It is also possible to control the speed with which the sample liquid is transported to the individual detection zones by means of the extent of capillarity.

It is of course also possible to extend the capillary channels of the second capillary-active zone in all three spatial dimensions.

The analytical test element according to the invention is preferably an analytical or diagnostic test carrier. It preferably contains reagents in the first and/or the second capillary-active zone for the detection of one or several analytes in a sample liquid.

Numerous embodiments of detection reagents are known to persons skilled in the art. Without intending to be complete, these include, among others, indicators, mediators, labelling substances, activators, biochemical reagents, enzymes, proteins, peptides, antigens or antibodies or fragments thereof, haptens and/or nucleic

acids. Such reagents are known to persons skilled in the art for numerous analytical and/or diagnostic applications. Although the following text often refers to "reagents," this term is also intended to include the use of only one reagent.

In addition to or instead of reagents in the true sense, one or both of the zones can contain other auxiliary substances such as buffers, wetting and spreading agents, stabilizers, magnetic particles and so forth.

The reagents and/or auxiliary substances can be incorporated by known methods into the capillary-active zones by impregnating the porous matrix of the first capillary-active zone or by coating at least a part of the surface of the capillaries of the second zone.

A further subject matter of the invention is a method for separating undesired sample components from a liquid sample which contains undesired sample components. For example, these may be undesired pigments in a colored sample liquid. But these are especially cellular, colored components of body fluids. They are especially preferably erythrocytes which are separated from whole blood.

In the method according to the invention, the liquid sample is first brought into contact with the capillary-active porous matrix material of the first capillary-active zone of an analytical element as described above according to the invention. The sample material is at least partially taken up by this matrix material. After it has passed through the matrix material, the sample liquid passes into the second capillary-active zone

whereby the liquid sample is essentially free of undesired sample components after having passed through the porous matrix material of the first capillary-active zone. Consequently, the first capillary-active zone serves as a filter or sieve for undesired sample components which would interfere with the subsequent reaction or measurement.

After the undesired sample components have been separated, it is then possible to qualitatively or quantitatively determine one or several analytes in the sample liquid in the sample material located in the second capillary-active zone. For this, the detection reagents contained in the first and/or second capillary-active zone react with the analyte or analytes that may be present in the sample liquid. In this way, a detectable signal is generated. Such a method is also a subject matter of the invention.

The use of an analytical test element according to the invention in one of the methods described above is also a subject matter of the invention.

Finally, a system which comprises an analytical test element according to the invention and a measuring instrument for detecting and optionally quantifying a detectable signal generated in the analytical test element is also a subject matter of the invention. Numerous embodiments of suitable measuring instruments are known to persons skilled in this field and do not require further elucidation here.

The advantages of the invention include the following:

- The sample liquid is not bound in a porous matrix in the analytical test element after separation of the undesired sample components. It is thus available for transmission and/or scattered light measurements which are usually not possible with conventional test elements.

- Any two-dimensional or three-dimensional transfer of the sample liquid in the capillary channels of the second capillary-active zone is possible. This leads to various possibilities for dosing and distributing the sample liquid to various detection zones.

The invention is elucidated in more detail by the following figures and examples.

Figure 1 shows a schematized, perspective view of a preferred embodiment of an analytical test element according to the invention.

Figure 2 shows a schematized cross-section through the test element of Figure 1.

Figure 3 shows a topview of an alternative embodiment of an analytical test element according to the invention.

The numbers in the drawing figures denote:

1,1'	test element
2,2'	base part
3,3'	membrane
4,4'	capillary channel
5	second capillary-active zone

6	first capillary-active zone
7,7'	sample application zone
8	overlap zone
9	transport direction
10	separation direction
11,11'	detection zone
12	detection field

Figures 1 and 2 show schematically a particularly preferred embodiment of an analytical test element (1) according to the invention. The test element (1) comprises a base part (2) and a membrane (3) which is mounted on it. A first capillary-active zone (6) is formed by the membrane (3). In this embodiment, the base part (2) contains a plurality of parallel capillary channels (4) which form a second capillary-active zone (5). The base part (2) is preferably an injection molded part in which the structures for the capillary channels (4) have already been incorporated in the injection molding process. Alternatively, the base part (2) can be a plastic foil in which the structures for the capillary channels (4) have been stamped or etched or on which the structures for the capillary channels (4) have been coated or printed.

Sample material which is to be examined with the test element (1) is applied onto the upper side of the membrane (3) which serves as a sample application zone (7). The porosity of the membrane (3) and the resulting capillary forces cause the sample material to be taken up into the membrane (3). Since the membrane (3) is in direct contact with a plurality of parallel identical capillary channels (4), the sample liquid passes from the membrane (3) into the capillary channels (4). Here it is moved, also as a result of the capillarity of the

second zone (5), in the capillary channels (4) from an overlap zone (8) lying between the first and second capillary-active zones (6 and 5) in a transport direction (9).

When the sample liquid passes through the membrane (3), sample components which would interfere with the subsequent use of the sample liquid, e.g. with the subsequent detection of a substance dissolved in the sample liquid, are removed from the sample liquid. The separation of the interfering components occurs in the vertical direction (in a separation direction (10)) in the shown embodiment of the test element (1) illustrated in Figures 1 and 2 according to the invention.

In the embodiment of the test element (1) according to the invention shown in Figures 1 and 2, a detection reaction in a detection zone (11) is preferably observed from above or through base part (2) if it is transparent. Detection reagents that may be required can either be impregnated in the membrane (3) or coated on the surfaces of the capillary channels (4).

The capillary channels (4) shown in Figure 1 which are open towards the top can of course be covered in the detection zone (11) by a preferably transparent cover (not shown) without impairing their function.

An alternative embodiment of a test element (1') according to the invention is shown schematically in Figure 3. The construction and function essentially correspond to the embodiment of the test element (1) according to the invention shown in Figures 1 and 2. However, in this case the capillary channels (4') lead

to three different detection fields (12) for typically different analytes which can be detected in one sample liquid. For example, the detection zone (11') can contain all reagents for the detection of glucose, cholesterol and lactate in blood. The detection fields (12) can themselves comprise conventional impregnated membranes or papers.

The capillary channels (4') of the embodiment shown in Figure 3 can be of different lengths and optionally transport different sample volumes at different speeds from the sample application zone (7') to the individual detection fields (12) in the detection zone (11'). However, it is also possible to design the capillary channels (4') geometrically in such a way that all detection fields (12) are supplied with identical sample volumes. Test elements with these possible variations could be constructed by persons skilled in the art without elucidation of further details here.

Example 1: Test element for separating plasma from whole blood

A test element structure corresponding to Figures 1 and 2 was manufactured. For this purpose, a rectangular transparent base part (length 10 mm, width 10 mm, height 2 mm) made of polycarbonate was injection-molded using a microinjection molding technique which contained 50 parallel capillary channels. The individual channels were identical to one another and had a width of about 30 µm and a depth of about 50µm. They extended over the entire surface of the base part. The surface of the base part was hydrophilized by plasma treatment on the side supporting the capillaries. A 4x4 mm^2 piece of a plasma separation membrane having a thickness of about 300 µm (available from PrimeCare B.V. of The Netherlands; pore size between 1.3 µm and 3.6 µm) was attached by mechanical pressure on that surface of the bottom part which had the capillary structures.

Example 2: Separation of plasma from whole blood

Ten µl whole blood were applied to the sample application side, i.e., the side of the membrane facing away from the capillary channels of the test element manufactured according to Example 1. The entire capillary channels were filled with plasma after about 10 seconds. It was possible to observe this filling process by the progress of the plasma front in the areas of the capillary channels that were not covered by the membrane.

Claims

We claim:

1. An analytical test element for examining a liquid sample, comprising a first and a second capillary-active zone which are in contact with one another and enable a liquid transfer in which the capillarity of the first capillary-active zone is caused by a capillary-active porous matrix material and enable liquid to pass spontaneously from the first capillary-active zone into the second capillary-active zone, wherein the second capillary-active zone contains one or several capillary gaps or channels which are at least partially overlapped by the porous matrix material of the first capillary-active zone.

2. The analytical test element of claim 1 wherein the capillary channel or capillary channels of the second capillary-active zone are open at least in the area where they are overlapped by the material of the first capillary-active zone so that liquid can pass from the first capillary-active zone into the second capillary-active zone through the openings.

3. The analytical test element of claim 1 wherein the capillary-active porous matrix material of the first capillary-active zone is capable of separating plasma or serum from a whole blood sample.

4. The analytical test element of claim 1 wherein the capillary-active porous matrix material comprises a membrane or a glass fiber fleece.

5. The analytical test element of claim 1 wherein the second capillary-active zone comprises an injection-molded part with capillary structures.

6. The analytical test element of claim 5 wherein the injection molded part comprises a transparent plastic.

7. The analytical test element of claim 1 wherein the second capillary-active zone comprises a carrier material in which capillary structures are stamped or etched.

8. The analytical test element of claim 1 wherein the second capillary-active zone comprises a carrier material on which structures are applied which define the capillaries.

9. The analytical test element of claim 1 wherein the surfaces of the capillary channels or gaps of the second capillary-active zone are at least partially hydrophilized.

10. The analytical test element of claim 1 wherein the second capillary-active zone contains regions of different capillarity.

11. The analytical test element of claim 1 wherein liquid is transported in the first capillary-active

zone essentially perpendicularly to the direction of liquid transport in the second capillary-active zone.

12. The analytical test element of claim 1 wherein the capillary-active porous material of the first capillary-active zone is in direct contact with the second capillary-active zone.

13. The analytical test element of claim 1 wherein the second capillary-active zone comprises a plurality of capillary channels that are parallel to one another.

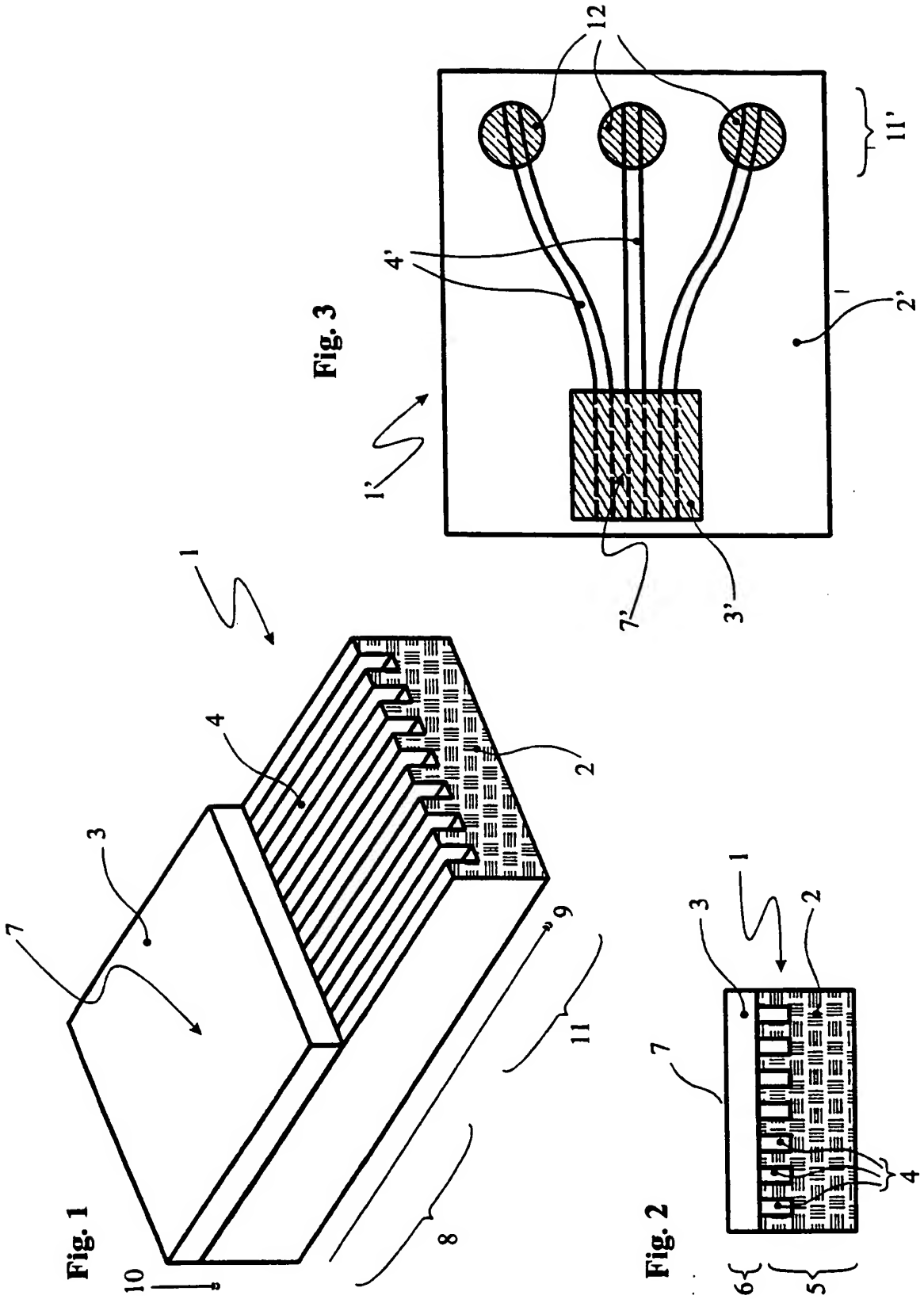
14. The analytical test element of claim 1 wherein at least one of the first and the second capillary-active zones contains a reagent for the detection of an analyte in a sample liquid.

15. A method for separating undesired sample components from a liquid sample containing undesired sample components wherein the liquid sample is brought into contact with the capillary-active porous matrix material of the first capillary-active zone of the analytical test element of claim 1, the liquid sample is at least partially taken up by this matrix material and, after passing through this matrix material, passes spontaneously into the second capillary-active zone whereby the liquid sample is essentially free of undesired sample components after passing through the porous matrix material of the first capillary-active zone.

16. A method for the qualitative or quantitative determination of one or several analytes in a liquid sample which contains undesired sample components wherein the liquid sample is brought into contact with the capillary-active porous matrix material of the first capillary-active zone of the analytical test element of claim 14, is at least partially taken up by this matrix material and, after passing through this matrix material, passes spontaneously into the second capillary-active zone whereby the liquid sample is essentially free of undesired sample components after passing through the porous matrix material of the first capillary-active zone and wherein the detection reagent contained in at least one of the first and the second capillary-active zones reacts with an analyte that may be present in the liquid sample to generate a detectable signal.

17. A system comprising the analytical test element of claim 1 and a measuring instrument capable of detecting and optionally quantifying a detectable signal produced in the analytical test element.

1/1



INTERNATIONAL SEARCH REPORT

Interr. .ial Application No
PCT/EP 00/09605

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01L3/00 //G01N33/52,C12Q1/56

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01L G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 17965 A (ABBOTT LAB) 6 July 1995 (1995-07-06) page 3, line 3 -page 4, line 2 page 10, line 33 -page 11, line 10 page 11, line 16 -page 11, line 17 page 11, line 29 -page 11, line 32	1,2,4-6, 8-12, 14-16
Y	page 12, line 11 -page 13, line 16 page 13, line 26 -page 14, line 7 page 19, line 20 -page 19, line 38	3,7,17
A	page 25, line 3 -page 25, line 8 page 26, line 2 -page 26, line 34 figures 3,8	3

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 January 2001	02/02/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Koch, A

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INTERNATIONAL SEARCH REPORT

Interr. nal Application No
PCT/EP 00/09605

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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